DRAFT DOCUMENT

PEST MANAGEMENT REGULATORY AGENCY
HEALTH CANADA

EDDE©

Electronic Dossier, Delivery, and Evaluation

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Livraison, Evaluation, Dossier Electronic

GUIDANCE FOR INDUSTRY

DURING PILOT STAGE

25 June 1999

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1.0 INTRODUCTION

In April 1997, the Pest Management Regulatory Agency (PMRA) implemented a cost recovery program and committed to improving processes and to reducing costs for the review of new Category A Dossiers. PMRA's target is to reduce costs of reviewing complex Dossiers by 40% in six years. To assist with achieving these commitments, the PMRA is investigating electronic information standards and tools with the objective of implementing an integrated Electronic Dossier, Delivery, and Evaluation (EDDE) capability.

This guidance specifically addresses the procedures to be followed during the pilot stage of the PMRA's EDDE capability. The purpose of these procedures is to ensure that the fundamental requirements of the PCP Act and Regulations continue to be observed and the interests of all participating parties are addressed while new approaches to the delivery and evaluation of dossiers are being tested. As part of the pilot process, these procedures, as well as the technologies deployed, will be assessed and recommendations made for implementation in a finalized EDDE capability and its associated guidance documentation.

Potential solutions for the provision of an integrated EDDE capability are being evaluated through an established philosophy based on the following principles: Industry/PMRA partnership; efficiency gain at both ends; user driven/not imposed; open and flexible standards; pilots to reduce risk and provide proof of concept validation; methodical evaluation of pilots; solutions providing for a range of capability; and cost effective implementation of solutions.

This Guidance Document includes a set of annexes grouped together in a document titled "Preliminary Statement of Evaluator Requirements". These annexes outline requirements based on the applicable Acts, Regulations, and working procedures and address such issues such as Electronic Dossier assembly and provision of electronic data formats that will contribute to the efficiency of PMRA evaluators. It is part of the objective for the Pilot Stage in the PMRA EDDE capability to refine, validate and finalize these requirements.

The PMRA's EDDE capability activities are international. Linkages are established with the US Environmental Protection Agency (EPA) - Office of Pesticide Programs (OPP), the European Union (EU), and the Organisation for Economic Co-operation and Development (OECD). There are three international venues for electronic dossier and evaluation capability activities:

1. Global Regulatory Information Technology (GRIT) group: This group reports its activities to the OECD Pesticides Forum. The formation of the GRIT group was announced at the November 1996 OECD Pesticide Forum meeting. Participants include the pesticide agencies from the United States, Canada, Germany,

Switzerland, United Kingdom, Australia, European Union member states, plus representation from the OECD Pesticide Forum secretariat, the European Crop Protection Association, the American Crop Protection Association and Canadian industry.

2. North American Free Trade Agreement (NAFTA) Technical Working Group (TWG), Regulatory Capacity Building: Joint projects in the Electronic Dossier, Delivery, and Evaluation environment are planned. Details of the projects are contained in the project plans for the NAFTA Technical Working Group on Pesticides.

3. CADDY Joint Data Transfer Steering Group: CADDY is an electronic Dossier interchange and archiving format which uses the TIFF (image-based) technology. The delivery media is a CD-ROM. Participants on the Joint Steering Group are: the European Crop Protection Association (ECPA), the American Crop Protection Association (ACPA), the Canadian pesticide industry, the EU member states, the PMRA and the U.S. EPA.

This guidance document has been developed, in part, by examination of existing guidance documents on electronic delivery of data available from the US FDA CDER[1a,b] (http://www.fda.gov/cder/guidance/index.htm), and for the CADDY specification[2a,b,c] (http://www.gcpf.org/). Relevant portions of these documents have been incorporated into this guidance.

2.0 PURPOSE OF THIS GUIDANCE

The purpose of this guidance is,

- to provide clear statement of the PMRA's business needs and goals with respect to Electronic Dossier Delivery and Evaluation capability; and

- to clearly establish the status and use of electronic Dossiers by the PMRA under the current pilot program for delivery of electronic Dossiers; and

- to encourage and facilitate the investigation of options for delivery and evaluation of electronic Dossiers by providing basic guidance to ensure that efforts expended by industry and the PMRA are productive and result in time and cost efficiencies.

2.1 PMRA Objectives

The PMRA has committed to achieving a 40% reduction in the cost of complex Dossier evaluation by the year 2003. Implementation of an integrated Electronic Dossier Delivery and Evaluation capability has the potential to deliver the majority of the required cost reduction. To this end, the objectives of the PMRA are,

- to pilot a variety of EDDE solutions and to share the results in international fora; and

- to develop guidance for Applicants which, while providing Applicants the flexibility to choose the means of electronic Dossier preparation, will enable the PMRA to obtain electronic Dossiers in a form which does not require specific electronic access tools and enables the functionality required for efficient electronic evaluation of Dossier data; and

- to implement an integrated Electronic Dossier, Delivery, and Evaluation environment Agency wide.

2.2 PMRA Vision for Electronic Dossier Delivery and Evaluation capability

The vision for the PMRA's EDDE capability is one that emphasizes the role of open standards and mainstream Internet technologies in the assembly and delivery of electronic dossiers. The rationale for this emphasis stems from the need for the EDDE capability to realize, in a compatible fashion, the following two requirements:

- The PMRA internal process for complex Dossier evaluation must be rationalized and the application of technology used to optimize the efficiency of PMRA staff; and,

- Applicants must be able to select and use technologies for the preparation of Dossiers that are compatible with their internal requirements and business objectives,

The main feature of the PMRA Vision for EDDE is the specification and implementation of an open, vendor-independent framework for the assembly, delivery, and evaluation of Electronic Dossiers. It is envisioned that this framework will exhibit the following features:

- the specification of a common mechanism for assembling Electronic Dossiers that leverages the Internet standard for encoding interchangeable metadata, the Extensible Markup Language (XML), and allows Applicants to use a variety of means for implementing this assembly mechanism;

- the specification of a commercially mainstream principle electronic data format that will act as the common basis for all Electronic Dossier Submissions and provide the basic data access and re-use/re-purposing capabilities;

- the specification of the processes to be followed for special cases where the Applicants must provide specialized native data formats to assist PMRA Evaluators in completing complex evaluations;

- the specification of application components and provision of implementation guidelines that will assist Applicants in complying with the requirements for assembling and delivering Electronic Dossiers under this framework; and,

- the deployment within PMRA of a set of application components, based on mainstream Internet technologies, that leverage this framework and provide substantial efficiency gains for PMRA Evaluators.

3.0 CONDITIONS AND REQUIREMENTS FOR THE PILOT DELIVERY OF ELECTRONIC DOSSIERS

For Dossiers which have an electronic component, pre-submission consultation with the PMRA is strongly recommended as soon as the compilation of an electronic Dossier is considered and well in advance of the actual date of delivery. The pre-submission consultation will serve to clarify needs and expectations, and the PMRA will offer assistance as appropriate.

3.1 Regulatory status of electronic Dossiers

At present, electronic Dossiers will be accepted by the PMRA on a pilot basis only. As such, electronically submitted Dossier data is considered separately from the paper based Dossier and does not form a formal part of the registration petition. Due to its pilots status, current acceptance of electronic Dossiers in their current form cannot be interpreted as setting any precedent for any parameter associated with EDDE in the future.

3.2 Regulatory data requirements for electronic Dossiers

3.2.1 Requirement for electronic Dossier

Delivery of Dossiers in electronic form is an option and not a requirement.

3.2.2 Regulatory data requirements

3.2.2.1 Scientific data

All normal regulatory requirements for Dossiers delivered to the PMRA under the PCP Act and Regulations apply to Dossiers which include electronic data.

3.2.2.2 Comprehensive Data Summaries

As stated in Regulatory Directive 97-01 and in section 5.1 (f) of the Registration Handbook, Comphrensive Data summaries must be submitted in valid WordPerfect format (version 5.x Windows through version 8.0) unless specified otherwise. If applicants wish to author the information in a different electronic environment, it is the applicant's responsibility to confirm that no text loss or format changes have occurred as a result of conversion to WordPerfect format. The document must have a hyperlinked Table of Contents. The Table of Contents should include study titles and all major study section titles. Tables and figures should also be included.

3.2.2.3 Required number of paper Dossier copies.

Applicants are required to submit a complete paper based Dossier with the required number of copies, as noted in the PCP Act and Regulations .

3.2.2.4 Required number of electronic Dossier copies

Original Dossier

For LAN based access to electronic Dossiers, two copies of the electronic Dossier need to be submitted. One copy will serve as the verification/backup/archive copy and will not be modified. The second copy will serve as the working evaluation copy and will be modified by addition of annotations, bookmarks, insertion of reference material/correspondence following data installation on LAN harddrives. These CD's are to be labelled as outlined in section 3.3.2 and 3.3.3.

For standalone evaluation applications, 10 copies of the electronic Dossier are required to provide an archive copy and a copy to each individual evaluator. These CD's are to be labelled as outlined in section 3.3.2.

Following data submissions

When submitting additional data to a Dossier, a complete new set of CD's, including the new data, are required. These CD's are to be labelled as outlined in section 3.3.2.

3.2.2.5 Cover Letter

Original Dossier

The Applicant should provide a cover letter as a PDF file named cover.pdf. This file should be located in the supplementary files directory under the DACO 0 sub-directory. This cover letter should also be included with the paper Dossier. The cover letter should include the following:

- **!** Description of the Dossier including appropriate regulatory information.

- **!** Description of which portions of the Dossier are presented only in paper, only in electronic format, or in both paper and electronic format.

- **!** Description of the electronic Dossier, including the type and number of electronic media used (e.g., three CD's), and the approximate size of the Dossier (e.g., 2 gigabytes).

- **!** Statement that the Dossier is virus free with a description of the software (name, version, date of virus signature update file, and company) used to check the files for viruses.

- **!** The points of contact for the application, including contact names for support/clarification for electronic Dossier installation and data access difficulties (See section 3.6).

Following data submissions

- **!** In addition to the information noted for original Dossier submissions, for subsequent data submissions affecting the original Dossier, a cover letter which clearly identifies which previously submitted data has been modified and/or which clearly identifies data new to the Dossier.

3.2.3 Identity with paper-based Dossier

All data contained within an electronic Dossier must exactly match the data contained in the equivalent portion of the paper Dossier. No data may be presented in the electronic Dossier which does not appear in the paper submission. However, the same data may be presented in an alternate format to provide more in-depth description or understanding (text description vs video or photomicrograph) or to enhance evaluators ability to analyze the data (spreadsheet data); (see associated guidance document: Preliminary Statement of Evaluator Requirements, Annex IV: Desirable electronic files and other review aids). Index headings in the electronic Dossier must replicate the headings used in the paper Dossier so that, when referral to the paper Dossier is necessary, equivalent Dossier/study data can be located quickly. To permit flexibility in presentation of the paper Dossier in electronic form, pagination does not have to be identical.

Applicants must submit a signed statement to indicate that the contents of the studies contained in the electronic Dossier are a true and accurate duplicate of the paper copies of the studies. The statement should read as follows:

"I certify that the enclosed electronic Dossier is a true and accurate duplicate of the enclosed paper copies of each study contained in this Dossier. I provide this

certificate in the knowledge that the making of a false or misleading statement either orally or in writing to an officer engaged in carrying out duties or functions under the *Pest Control Products Act* is an offence that is punishable by fine or imprisonment."

Any deviation from the above statement must be discussed and agreed to during the Pre-Submission Consultation.

3.3 Delivery of electronic Dossiers and performance standards

3.3.1 Pre-Submission consultation

For Dossiers which have an electronic component, pre-Submission consultation with the PMRA is strongly recommended as soon as the compilation of an electronic Dossier is considered and well in advance of the actual date of delivery. The pre-submission consultation will serve to clarify needs and expectations, and the PMRA will offer assistance as appropriate.

3.3.2 Delivery process

Delivery of electronic Dossiers follows the normal paper-based submission process. Transfer of electronic Dossiers to the PMRA using compact discs (CD's) is preferred. Package all CD's in such a manner as to ensure that they arrive in a usable condition. Attach labels to the CD's, including the CD jewel cases. Label information should include the following:

- **!** Proprietary and common name (for technical actives)
- **!** Company name
- **!** Dossier serial number, if applicable
- **!** Delivery date: in the format of DD-MMM-YYYY (for example, 01-Jan-2000)
- **!** Number CD's from 1 of #; Version 1 through # of #; Version 1 for the original Dossier

3.3.3 Delivery of corrected or additional data

Submission of corrected or additional data for electronic Dossiers is subject to normal regulatory requirements. For each subsequent submission to the PMRA, a complete new set of CD volumes is required, labelled as outlined in section 3.3.2 with a cover letter as outlined in section 3.2.2. The Dossier version number should be increased as appropriate, using whole numbers only.

3.3.4 Electronic Dossier screening

In addition to the normal screening process for paper Dossiers, screening electronic Dossiers involves verification of:

- presence of all electronic data media intended as part of the submission (ie presence of 6 of 6 CD's).
- virus free status on all electronic data files submitted.
- presence of required electronic data (index, label, comprehensive data summary).
- verification of identity with the paper copy Dossier by noting presence of the required certification of data identity letter.
- verification of data legibility and utility for evaluation purposes.
- verification of agreements made during any pre-submission consultation as they affect the electronically submitted data.

Due to the pilot status of electronic Dossiers, formal Level B and C deficiency letters will not be issued from the PMRA submission screening group based on elements associated with the electronic Dossier. While under pilot status, feedback on th pilot will be issued by the Business Line Improvement Section.

The screening process for electronic data continues to evolve as experience is gained in pilots with electronic Dossiers. Revisions to this guidance document will be made as experience is gained.

3.3.5 Performance standards

Performance standards for completion of Dossier evaluation and regulatory decision are as per the Management of Submissions Policy.

3.4 Use of electronic data within the PMRA during the pilot phase

Every attempt will be made to utilize electronically available data during evaluation of the Dossier. If, however, unexpected issues arise in the use of the electronic data that are of a sufficient nature and duration that PMRA performance standards could be jeopardized, evaluation will revert to the traditional paper based evaluation method. Applicants will be advised when this occurs.

Electronic Dossiers will be used by the PMRA for the purpose of determining:

- efficiency gains which may result from availability of Dossier data in electronic format.
- impact on the PMRA information technology infrastructure.
- electronic archiving processes and requirements.

3.5 Security of electronic data within the PMRA

The PMRA handles all Dossier data, paper and electronic, in a manner appropriate to its confidential nature. The PMRA provides a secure physical facility for storage and evaluation of data.

3.5.1 Locally installed data access tools

Where Dossier data is accessed directly at evaluator workstations, the data access software is required to provide a password protection feature. In addition, evaluators are required to maintain Dossier data CD's under lock and key at their workstations.

3.5.2 LAN based data access tools

The PMRA operates a secure LAN system. LAN based Dossiers are loaded onto a secure server which, along with the LAN system servers, is maintained in a locked room accessible only to authorized staff. Access to the electronic Dossier requires first password controlled access to the PMRA LAN, followed by a second password controlled access to the Dossier data server.

3.6 Support of pilot electronic Dossiers

The PMRA is trying to solicit and pilot a variety of EDDE solutions. Due to the potential variety of solutions submitted under this pilot program, the PMRA requires points of contact for support in the event of electronic Dossier installation and data access difficulties. The requirement for support is expected to be on a case-by-case basis, and should be discussed during the pre-submission consultation meeting.

Under the current pilot status of EDDE, if difficulties arise in the use of the electronic data of a sufficiently serious nature and duration that PMRA performance standards could be jeopardized, evaluation will revert to the traditional paper based evaluation method.

4.0 PMRA CONTACTS

For advice or clarification of issues related to electronic Dossiers contact either

Cameron Bowes
Room E555
Sir Charles Tupper Building,
2250 Riverside Drive,
Address Locator: 6605E
Ottawa, Ontario, K1A 0K9
ph: 613-736-3514
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Address Locator: 6607D
Ottawa, Ontario, K1A 0K9
ph: 613-736-3696
fx: 613-736-3699
email: ckrogh@pmra-arla.hc-sc.gc.ca

5.0 REFERENCES

1a: Guidance for Industry: Providing Regulatory Submissions in Electronic Format — General Considerations; U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologic Evaluation and Research (CBER) and Center for Biologics Evaluation and Research (CBER), January 1999

1b: Guidance for Industry: Providing Regulatory Submissions in Electronic Format — NDAs; U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER), January 1999

Further information can be obtained at http://www.fda.gov/cder/guidance/index.htm

2a: Joint CADDY Steering Group. Format Specification CADDY 1.1, Document Interchange Format for PPP Registration Applications, September 1997.

2b: Joint Data Transfer Steering Group Software Specification - CADDY Standard Retrieval Software, Version 0.3, February 1997.

2c: PSI AG, Supplemental Specification, CADDY Retrieval Software, August 1997. Further information can be obtained at http://www.gcpf.org/